

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)			
(51) International Patent Classification ⁶ :			(11) International Publication Number: WO 99/25320
A61K 9/127, 48/00, C12N 15/88		A1	(43) International Publication Date: 27 May 1999 (27.05.99)
(21) International Application Number: PCT/US98/24657 (22) International Filing Date: 19 November 1998 (19.11.98)			BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD,
(30) Priority Data: 60/066,188 60/083,175	19 November 1997 (19.11.9 27 April 1998 (27.04.98)	97) T	SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW) Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM) European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR

(71)(72) Applicants and Inventors: CHANG, Esther, H. [US/US]; 7508 Vale Street, Chevy Chase, MD 20815 (US). XU, Liang [CN/CN]; 1200 N. Queen Street #608, Arlington, VA 22209 (US). PROLLO, Kathleen [US/US]; 2001 N. Adams Street #1031, Arlington, VA 22201 (US).

(74) Agents: NEWLAND, Bart, G. et al.; Rothwell, Figg, Ernst & Kurz, Columbia Square, Suite 701 East, 555 13th Street N.W., Washington, DC 20004 (US). European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of

(54) Title: TARGETED LIPOSOME GENE DELIVERY

Targeted ligand-liposome-therapeutic molecule complexes (vectors) for the systemic delivery of the therapeutic molecule to various target cell types including cancer cells such as squamous cell carcinoma of the head and neck, breast and prostate tumors. The preferred ligands, folate and transferrin, target the liposome complex and facilitate transient gene transfection. The systemic delivery of complexes ingands, totate and transferrin, target the liposome complex and facilitate transferring gene transferring. The systemic delivery of complexes containing DNA encoding wild-type p53 to established mouse xenografts markedly sensitized the tumors to radiotherapy and chemotherapy. The combination of systemic p53 gene therapy and conventional radiotherapy or chemotherapy resulted in total tumor regression and long term inhibition of recurrence. This cell-specific delivery system was also used in vivo to successfully deliver, via intravenous administration, small DNA molecules (oligonucleotides) resulting in chemosensitivity and xenograft growth inhibition. Other therapeutic molecules including intact viruses can be encapsulated in a complex and targeted in accordance with the invention molecules, including intact viruses, can be encapsulated in a complex and targeted in accordance with the invention.